

### **REMARKS**

The Applicants respectfully request further examination and consideration of the claims in view of the above amendments and the arguments set forth fully below. Claims 1-14 were pending in this application. Within the Office Action, Claims 1-14 have been rejected. By the above amendment, Claims 1, 10, 13 and 14 have been amended and Claim 11 has been canceled. Accordingly, Claims 1-10 and 12-14 are currently pending in this application.

#### **Election/Restriction**

Within the Office Action, the Claims 1-22 have been subject to a restriction and/or election requirement. The Restriction Requirement indicates that Group I claims (drawn to an optical detection method) and Group II claims (drawn to an optical detection system for a protein microarray) are directed to distinct inventions. The Applicants note that Group I claims include Claims 1-14 and Group II claims include Claims 15-22. The Applicants elect, without traverse, Group I including Claims 1-14 for continued prosecution. The Applicants expressly reserve the right to file a divisional application directed toward the non-elected group.

#### **Rejections Under 35 U.S.C. § 102**

Within the Office Action, Claims 1-4, 6-10 and 12 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,143,495 to Lizardi et al. (hereinafter "Lizardi") and Claims 1-3, 5, 7, 10 and 11 have been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,800,453 to Labaer et al. (hereinafter "Labaer"). The Applicants respectfully disagree. Reconsideration of the present application is respectfully requested.

It is alleged within the Office Action that Lizardi teaches a method for amplifying nucleic acid sequences based on the presence of a specific target sequence or analyte with high specificity and sensitivity. By coupling a nucleic acid tag such as open circle probes (OCP) to a specific binding molecule, such as an antibody, rolling circle amplification of the nucleic acid tag can be used to detect analytes in a sample. Rolling circle amplification is accomplished by a rolling circle replication primer that is complementary to the primer complement portion of the OCP. To aid in detection and quantitation of nucleic acids amplified by using RCA and RCT, detection labels can be directly incorporated into amplified nucleic acids or can be coupled to detection molecules. Detection labels include radioactive isotopes, fluorescent molecules, phosphorescent molecules, enzymes, antibodies, and ligands.

In this aspect, the key point of the present invention is using the nanogold combining the nucleic acid probe as the detection molecule without the detection labels. This is not taught by Lizardi.

In addition, the above technical scheme has several benefits such as: a) the nanogold is stable; b) the nanogold can be detected by naked eyes or normal optical instruments; c) the nanogold expresses without photobleaching; d) the cost of the nanogold is low; and e) the nanogold can be reused.

The independent Claim 1 includes the step of detecting said amplified signal via a nanogold probe and a quantum dot. As discussed in detail above, this is not taught by Lizardi. For at least these reasons, the independent Claim 1 is allowable over the teachings of Lizardi.

After comparing the presently claimed invention and the teachings of Labaer, it is noticed that they are completely different methods for detecting peptides array. The key point of Labaer is picking up a selected clone complementary to the target peptide, which has specific tags or affinity molecules for recognition. The next step is translating the clone into the complementary peptide and hybridizing with the target peptide. Then, using the specific antibody coupling to a derivatized substrate or the specific affinity molecule binds to the complementary peptide for amplifying the recognizing signal. Finally, using the art-known method exhibits the result.

The present invention uses a capture molecule coupling to a specific nucleic acid sequence. When recognizing the target, using the rolling circle amplification amplifies the specific nucleic acid sequence. Using the nanogold coupling to a complementary nucleic acid sequence binds to the amplified nucleic acid sequence, and then observes the result.

The presently claimed invention and the teachings of Labaer belong to two different systems. For at least these reasons, the independent Claim 1 is allowable over the teachings of Labaer.

By the above amendment, Claim 11 has been canceled. Claims 2-10 and 12-14 are all dependent upon the independent Claim 1. As discussed above, the independent Claim 1 is allowable over the teachings of Lizardi and Labaer. Accordingly, Claims 2-10 and 12-14 are all also allowable as being dependent upon an allowable base claim.

### **Rejections Under 35 U.S.C. § 103**

Within the Office Action, Claim 11 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over Lizardi in view of U.S. Patent No. 6,480,791 to Strathmann (hereinafter "Strathmann"), Claims 13 and 14 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Lizardi in view of U.S. Patent No. 6,361,944 to Mirkin et al. (hereinafter

“Mirkin”) and further in view of U.S. Patent No. 6,579,726 to Natan et al. (hereinafter “Natan”), Claim 11 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over Labaer in view of Strathmann and Claims 13 and 14 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Labaer in view of Mirkin and further in view of Natan.

It is asserted within the Office Action that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the fluorescent labels of Lizardi with quantum dots because Strathmann teaches that fluorescent labels and quantum dots are functional equivalents as nucleic acid labels. Neither Strathmann nor Lizardi includes any teaching or suggestion for substituting the fluorescent labels in Lizardi with quantum dots. Any allegation beyond the teachings of the prior art is hindsight. Based on these comparisons, it is clear that the present application is very distinguishable from the combination of Lizardi and Strathmann.

It is also asserted within the Office Action that it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the 5' end of the oligonucleotides with an -SH group as taught by Mirkin in the invention of Lizardi, as Mirkin teaches that such a modification provides the advantage of strongly attaching the oligonucleotides to the gold nanoparticles; and it would also have been obvious to one of ordinary skill in the art at the time of the invention to utilize spherical gold nanoparticles, as taught by Natan, in the method of Lizardi in order to achieve a 100,000 fold increase in sensitivity by using detection means such as SPR. Neither Lizardi nor Mirkin teach or suggest modifying the 5' end of the oligonucleotides with an -SH group. Any allegation beyond the teachings of the prior art is hindsight.

Furthermore, the SPR in the present application is just an example for illustrating how sensitive the present invention could be. One of the benefits of the present invention is that the experimental result could be observed by the naked eyes. Based on the above comparisons, it is clear that the present invention is very distinguishable from the teachings of Lizardi, Mirkin and Natan.

Further, by the above amendment, Claim 11 has been canceled. Claims 13 and 14 are both dependent upon the independent Claim 1. As discussed above, the independent Claim 1 is allowable over the teachings of Lizardi and Labaer. Accordingly, Claims 13 and 14 are both also allowable as being dependent upon an allowable base claim.

For the reasons given above, the Applicants respectfully submit that the claims are in a condition for allowance, and allowance at an early date would be appreciated. Should the Examiner have any questions or comments, the Examiner is encouraged to call the undersigned at (408) 530-9700 to discuss the same so that any outstanding issues can be expeditiously resolved.

Respectfully submitted,  
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CERTIFICATE OF MAILING (37 CFR § 1.8(a))

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